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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/717,378	11/19/2003	Aquilur Rahman	224491	6704

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LEYDIG VOIT & MAYER, LTD
TWO PRUDENTIAL PLAZA, SUITE 4900
180 NORTH STETSON AVENUE
CHICAGO, IL 60601-6780

EXAMINER	
RUSSEL, JEFFREY E	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 03/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/717,378	RAHMAN ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20031119*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. Applicant is advised that should claim 23 be found allowable, claim 46 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claims 23 and 46 are identical in scope. It is believed that claim 46 should instead depend upon claim 34.

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 24-45 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 153-238 of copending Application No. 10/424,258. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '258 application anticipate the instant claims. SN-38 is an active metabolite of irinotecan, and thus is a camptothecin. With respect to instant claims 26-28, in view of the similarity in composition and method steps, the cardiac tissue accumulation, the plasma concentration curve, and the plasma half life will inherently be the same for the claimed compositions and methods of the '258 application as are recited in Applicants' claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

3. Claims 24-45 are directed to an invention not patentably distinct from claims 153-238 of commonly assigned Application No. 10/424,258. Specifically, see the above provisional obviousness-type double patenting rejection.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned Application No. 10/424,258, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. v. Quigg, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In re Clinton, 188 USPQ 365, 367 (CCPA 1976); In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

5. Claims 24-32, 34-38, and 40-44 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 95/08986. The WO Patent Application '986 teaches camptothecin in multilamellar or unilamellar vesicles for use in treating cancer. The vesicles can be comprised of negatively, positively, or neutrally charged lipids, including cardiolipin, alpha-tocopherol,

phosphatidylcholine, cholesterol, and phosphatidyl serine, and can have sizes preferably less than 0.2 microns for intravenous administration. The camptothecin thus formulated has reduced toxicity and improved efficacy. See, e.g., the Abstract; page 3, lines 6-9; page 5, lines 14-17; page 6, lines 26-27 and 33-35; page 7, lines 6-7; and claims 1, 9, and 27. With respect to instant claims 26-28, in view of the similarity in composition and method steps, the cardiac tissue accumulation, the plasma concentration curve, and the plasma half life will inherently be the same for the compositions and methods of the WO Patent Application '986 as are recited in Applicants' claims. Sufficient evidence of similarity is deemed to be present between the methods and compositions of the WO Patent Application '986 and Applicants' claimed methods and compositions to shift the burden to Applicants to provide evidence that the claimed methods and compositions are unobviously different than those of the WO Patent Application '986.

6. Claims 33 and 45 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 95/08986 as applied against claims 24-32, 34-38, and 40-44 above, and further in view of Ahmad et al (U.S. Patent Application Publication 2003/0215492), Rahman (U.S. Patent No. 6,146,659), or Rahman et al (U.S. Patent No. 5,648,090). The WO Patent Application '986 does not disclose a pharmaceutical composition comprising a mixture of multilamellar and unilamellar vesicles. Ahmad et al (see paragraph [0008]), Rahman (see column 3, lines 50-51), and Rahman et al (see claim 11) disclose administering antineoplastic agents in pharmaceutical compositions comprising a mixture of multilamellar and unilamellar vesicles. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer the camptothecin of the WO Patent Application '986 in combination with a mixture of multilamellar and unilamellar vesicles because Ahmad et al,

Rahman, and Rahman et al disclose this to be a known type of liposome formulation for administering antineoplastic agents, because it is routine in the pharmaceutical arts to administer known therapeutic agents using different pharmaceutical forms which are themselves known in the art, and because the resulting pharmaceutical composition has only the expected antineoplastic activity.

The subject matter disclosed in Ahmad et al and relied upon in the above rejection is disclosed in provisional application 60/247,306, upon which Ahmad et al claim priority under 35 U.S.C. 119(e). See, e.g., page 2, lines 18-19, of the provisional application. Accordingly, Ahmad et al, which has a different inventorship and an earlier effective filing date than the instant application, is prior art against instant claims 33 and 45 under 35 U.S.C. 102(e).

7. Claim 39 is rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 95/08986. Application of the WO Patent Application '986 is the same as in the above rejection of claims 24-32, 34-38, and 40-44. The WO Patent Application '986 does not teach vesicles having a size of about 0.1 micron or less. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal vesicle sizes for the vesicles of the WO Patent Application '986, because the reference teaches that vesicle size is a result-effective variable and it is routine in the art to determine and optimize such variables.

8. Claims 1-9, 11-21, 23, and 46 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 95/08986 as applied against claims 24-32, 34-38, and 40-44 above, or as applied against claim 39 above, and further in view of the Sadzuka article (Cancer Letters, Vol. 127, pages 99-106) or the Sadzuka et al article (Current Drug metabolism, Vol. 1, pages 31-

48). The WO Patent Application '986 does not teach using irinotecan as the camptothecin in the vesicles. The Sadzuka article and the Sadzuka et al article teach the administration of irinotecan entrapped in a liposome. It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to use the irinotecan of the Sadzuka article or the Sadzuka et al article as the source of the camptothecin in the vesicles of the WO Patent Application '986 because the WO Patent Application '986 embraces the use of any camptothecin analog in its vesicles, and because the Sadzuka article and the Sadzuka et al article suggest that irinotecan is especially suitable for administration using such a carrier. With respect to the cardiac tissue accumulation, the plasma concentration curve, and the plasma half life specified in the instant claims, these results are fully consistent with and are deemed to be suggested by the benefits described by the WO Patent Application '986, the Sadzuka article, and the Sadzuka et al article for their liposome-based formulations, i.e. reduced toxicity, improved efficacy, increased plasma concentration, and improved tissue distribution.

9. Claims 10 and 22 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 95/08986 in view of the Sadzuka article (Cancer Letters, Vol. 127, pages 99-106) or the Sadzuka et al article (Current Drug metabolism, Vol. 1, pages 31-48) as applied against claims 1-9, 11-21, 23, and 46 above, and further in view of Ahmad et al (U.S. Patent Application Publication 2003/0215492), Rahman (U.S. Patent No. 6,146,659), or Rahman et al (U.S. Patent No. 5,648,090). The WO Patent Application '986, the Sadzuka article, and the Sadzuka et al article do not disclose a pharmaceutical composition comprising a mixture of multilamellar and unilamellar vesicles. Ahmad et al (see paragraph [0008]), Rahman (see column 3, lines 50-51), and Rahman et al (see claim 11) disclose administering antineoplastic

agents in pharmaceutical compositions comprising a mixture of multilamellar and unilamellar vesicles. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer the irinotecan of the WO Patent Application '986 as modified above by the Sadzuka article or the Sadzuka et al article in combination with a mixture of multilamellar and unilamellar vesicles because Ahmad et al, Rahman, and Rahman et al disclose this to be a known type of liposome formulation for administering antineoplastic agents, because it is routine in the pharmaceutical arts to administer known therapeutic agents using different pharmaceutical forms which are themselves known in the art, and because the resulting pharmaceutical composition has only the expected antineoplastic activity.

The subject matter disclosed in Ahmad et al and relied upon in the above rejection is disclosed in provisional application 60/247,306, upon which Ahmad et al claim priority under 35 U.S.C. 119(e). See, e.g., page 2, lines 18-19, of the provisional application. Accordingly, Ahmad et al, which has a different inventorship and an earlier effective filing date than the instant application, is prior art against instant claims 33 and 45 under 35 U.S.C. 102(e).

10. Claims 24-45 are rejected under 35 U.S.C. 102(e) as being anticipated by Ahmad et al (U.S. Patent Application Publication 2003/0215492). Ahmad et al teach treating cancer in a human by administering SN-38 complexed with a liposome. The liposome can be comprised of negatively, positively, or neutrally charged lipids, including cardiolipin, tocopherol, phosphatidylcholine, cholesterol, dipalmitoyl phosphatidyl choline, and phosphatidyl serine, and can have sizes preferably less than 0.1 microns. The liposome complexes can comprise mixtures of multilamellar and unilamellar vesicles. SN-38 is an active metabolite of irinotecan, and thus is a camptothecin. See, e.g., paragraphs [0002] and [0008]; Examples 1-4; and claims 1-6 and

17-26. With respect to instant claims 26-28, in view of the similarity in composition and method steps, the cardiac tissue accumulation, the plasma concentration curve, and the plasma half life will inherently be the same for the compositions and methods of Ahmad et al as are recited in Applicants' claims. Sufficient evidence of similarity is deemed to be present between the methods and compositions of Ahmad et al and Applicants' claimed methods and compositions to shift the burden to Applicants to provide evidence that the claimed methods and compositions are unobviously different than those of Ahmad et al.

The subject matter disclosed in Ahmad et al and relied upon in the above rejection is disclosed in provisional application 60/247,306, upon which Ahmad et al claim priority under 35 U.S.C. 119(e). See, e.g., page 1, lines 10-13; page 2, lines 18-19; page 5, lines 17-23; Examples 1-4; and claims 1-4, 8-18, 20-27, and 32-34; of the provisional application. Accordingly, Ahmad et al, which has a different inventorship and an earlier effective filing date than the instant application, is prior art against instant claims 24-45 under 35 U.S.C. 102(e).

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Bruce Campell can be reached at (571) 272-0974. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.

Jeffrey E. Russel
Primary Patent Examiner
Art Unit 1654

JRussel
March 1, 2005